REMARKS

Favorable reconsideration of the subject application is respectfully requested in view of the following remarks. Claims 1, 3-6, 9-11, 13-19 and 20-23 are pending. Claims 1, 3-6, 9-11 and 15-19 have been withdrawn from consideration. With the above amendment, claims 13 and 14 have been canceled. The above amendments are not to be construed as acquiescence with regard to the Examiner's rejections and are made without prejudice to prosecution of any subject matter removed or modified by this amendment in a related divisional, continuation or continuation-in-part application.

Priority

The Action contends that the presently claimed polypeptide sequence of SEQ ID NO:176 was not disclosed in parent applications preceding Application No. 09/466,396. Therefore, the Action asserts that the present application is entitled only to the priority date of Application No. 09/466,396, or December 17, 1999.

Without acquiescing to the Action's determination, Applicants have amended the Cross Reference to Related Applications paragraph on the first page of the specification and submit herewith a supplemental ADS reflecting the new priority claim.

Rejection Under 35 U.S.C. § 112, second paragraph (indefiniteness)

Claims 13 and 14 stand rejected under 35 U.S.C. § 112, second paragraph as allegedly being indefinite. In particular, the Action alleges that the claims are incomplete for omitting essential steps.

Without acquiescing to the rejection, Applicants have canceled claims 13 and 14. Applicants submit that the above amendments obviate and overcome the rejection. Accordingly, Applicants respectfully request withdrawal of the rejection under 35 U.S.C. § 112, second paragraph.

Rejection Under 35 U.S.C. § 112, first paragraph (written description)

Claims 13, 14, 20, and 21 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking written description. In particular, the Action asserts that the claims read on a genus of polypeptides comprising an amino acid sequence having at least 90% identity to the sequence of SEQ ID NO:176 and therefore the claims allegedly encompass adding unknown and unidentified amino acid sequences to the 5' or 3' end and/or within SEQ ID NO:176 that results in unknown and unidentified polypeptides having different biological functions. The Action also alleges that the specification fails to disclose any structural feature that is essential to the biological function of the polypeptide of SEQ ID NO:176. The Action further contends that since the specification fails to provide any common structural attributes that identify the members of the genus and since the genus is highly variant, the polypeptide sequence of SEQ ID NO:176 is insufficient to describe the genus.

Applicants respectfully traverse the rejection on the following grounds.

Applicants submit that the claimed genus of polypeptides is described in the specification as filed. In particular, Applicants describe that the claimed polypeptide of SEQ ID NO:176 has a lung-tumor expression profile. The PTO Guidelines on Written Description are quite clear that:

> An applicant may also show that an invention is complete by disclosure of sufficiently detailed relevant identifying characteristics which provide evidence that applicant was in possession of the claimed invention, *i.e.*, complete or partial structure, other physical and/or chemical functional characteristics when coupled with a known or disclosed correlation between function and structure of some combination of such characteristics. (Federal Register, Vol. 66, No. 4, June 5, 2001; page 1106, first column)

Applicants submit that a sufficient and relevant identifying characteristic shared by members of the currently claimed genus is the structural characteristic of having at least 90% identity to SEQ ID NO:176. Applicants further submit that the skilled artisan would readily appreciate that Applicants were indeed in possession of the claimed invention at the time of filing, in particular when this structural characteristic is combined with the functional characteristic shared by members of the currently claimed genus, *i.e.*, their ability to stimulate T cells that are specific for an amino acid sequence present in the polypeptide set forth in SEQ ID

NO:176. These common structural and functional attributes of the claimed polypeptides are recited in the claims.

To accept the Action's position that Applicant was only in possession of an immunogenic composition comprising the specific species of SEQ ID NO:176 would thus inappropriately exclude an entire class of polypeptides related to SEQ ID NO:176 that the skilled individual would appreciate were in Applicants' possession at the time of filing. For example, given the Applicants' discovery that this polypeptide is expressed in lung tumor tissue relative to normal lung tissue, it is submitted that the skilled artisan would immediately recognize that the Applicants were in possession of much more than the specific sequence of SEQ ID NO:176. Rather, in view of this disclosure, and further in view of the level of general knowledge in this art, the skilled artisan would understand and expect that an entire class of polypeptides structurally related to SEQ ID NO:176, *e.g.*, sequences having at least 90% identity to SEQ ID NO:176, would also be useful in the context of the Applicants' invention, despite the fact that they are not identical to the specific sequence of SEQ ID NO:176. The skilled artisan would indeed fully expect that such sequences related to SEQ ID NO:176 could be used, for example, in generating, *e.g.*, T cells having specificity for a polypeptide sequence of SEQ ID NO:176, despite the fact that the sequences are not identical with the specific sequence of SEQ ID NO:176. This understanding and expectation on the part of the skilled artisan is submitted to be soundly based upon fundamental scientific principles.

Applicants submit that one skilled in the art would recognize, in light of the instant disclosure, an identifying characteristic shared by members of the claimed genus and that Applicant was in possession of this claimed genus at the time the application was filed.

Furthermore, Applicants respectfully note that specific epitopes of the L523S lung tumor antigen set forth in SEQ ID NO:176 that stimulate T cells, were identified and described in the specification as filed for example, at page 146, line 24 - page 147, line 7. Therefore, the skilled artisan would readily appreciate that amino acids in the remainder of the molecule, *i.e.*, outside of the amino acid residues making up the epitopes, could readily be changed without affecting the ability of the epitope to stimulate T cells. Further, as stated in specification as filed, variants of the defined epitopes can be produced wherein one or more amino acids are altered such that there is no effect on the ability of the peptides to elicit a T cell response. Thus,

contrary to the assertions of the Action, Applicants submit that the specification describes the claimed invention.

With regard to structural features essential to biological function, Applicants submit that it was known in the art at the time of filing that the polypeptide of SEQ ID NO:176 contains four KH domains, domains found in a subset of RNA-binding proteins, as discussed in the Mueller-Pillasch reference cited on page 13 of the Action. Nevertheless, Applicants submit that knowledge of the biological function is not necessary or even relevant for using the polypeptide or variants thereof to stimulate T cells. To generate T cells, full-length protein or overlapping peptides, generally from 8-20 amino acids in length, spanning the entire length of a given protein, can be used to pulse antigen-presenting cells, as described in the specification, for example, at page 146, line 24 - page 147, line 7 and elsewhere. Alternatively, as described for example, at page 167, line 5 - page 168, line 2, the antigen-presenting cells can be transduced or otherwise genetically modified to express a protein or peptide of interest. The protein or peptides are processed by the antigen-presenting cells such that short, linear peptides are presented to T cells in the context of MHC molecules on the surface of the antigen-presenting cells. This process is independent of the biological function of the polypeptide. Therefore, Applicants submit that it is not necessary to describe a biological function of the claimed polypeptide of SEQ ID NO:176.

In view of the above remarks, Applicants respectfully submit that the claimed invention satisfies the written description requirement under 35 U.S.C. § 112, first paragraph and urge that the rejection may be properly withdrawn.

Rejection Under 35 U.S.C. § 112, first paragraph (enablement)

Claims 13, 14, 20, and 21 stand rejected under 35 U.S.C. § 112, first paragraph as allegedly lacking enablement. Specifically, the Action alleges that, while the specification is enabling for an immunogenic composition comprising SEQ ID NO:176, or comprising residues 37-55 or 41-51 of SEQ ID NO:176, the specification allegedly does not reasonably provide enablement for an immunogenic composition comprising any portion of SEQ ID NO:176 other than the disclosed residues 37-55 or 41-51 of SEQ ID NO:176, nor an immunogenic composition comprising a polypeptide having at least 90% identity to SEQ ID NO:176 or a portion thereof,

nor methods for simulating an immune response or treating a lung cancer in a patient using said immunogenic compositions comprising a polypeptide having at least 90% identity to SEQ ID NO:176 or a portion thereof. The Action contends that the claims encompass adding unknown and unidentified amino acid sequence to the ends or within the claimed polypeptide of SEQ ID NO:176 that result in various unknown and unidentified polypeptides having different biological functions. The Action cites numerous references to support the contention that the ability to generate antibodies depends on the three dimensional structure of the protein and further that determining the three dimensional structure of a protein does not necessarily reveal anything about its function. Addtionally, the Action asserts that the specification fails to provide guidance and evidence for whether administration of a composition comprising the claimed polypeptides or a portion thereof can stimulate an immune response in a patient.

Applicants respectfully traverse this rejection on the following grounds.

As an initial matter, Applicants respectfully point out that the invention is directed to immunogenic compositions for inducing predominantly Th1-type (*i.e.* T cell) responses and wherein the polypeptides contain an amino acid sequence that is capable of stimulating T cells that are specific for an amino acid sequence present in the polypeptide set forth in SEQ ID NO:176. Accordingly, Applicants reiterate that the biological function of the claimed polypeptides is not relevant to its ability to induce a T cell response. As discussed above, to generate T cells, full-length protein or overlapping peptides spanning the entire length of a given protein, can be used to pulse antigen-presenting cells. Alternatively, the antigen-presenting cells can be transduced or otherwise genetically modified to express a protein or peptide of interest. The protein or peptides are processed (*i.e.*, degraded) by the antigen-presenting cells such that short, linear peptides are presented to T cells in the context of MHC molecules on the surface of the antigen-presenting cells. This process is largely independent of the biological function of the polypeptide. Moreover, the peptides presented by the APC and recognized by the T cells are generally short, linear peptides generated by degradative processes within the cell. As such, the three dimensional structure of a protein, while certainly relevant for antibody determinants, is generally not relevant in the context of T cell epitopes.

Applicants have demonstrated in the instant disclosure that human T cells react specifically with the L523S lung tumor antigen set forth in SEQ ID NO:176, and portions thereof

(see Example 14, page 146, line 24-page 147, line 7). In view of this disclosure by Applicants the skilled artisan would understand that L523S was demonstrated to be an antigen effective for stimulating an L523S-specific T cell response in humans. The skilled artisan would further understand, in view of this disclosure, that sequences sharing a high degree of structural identity with SEQ ID NO:176, *e.g.*, sequence having at least 90% identity with SEQ ID NO:176, would also be capable of stimulating T cells specific for the sequence of SEQ ID NO:176, as currently claimed. For example, the skilled artisan would understand that these highly related sequences, *e.g.*, sequences having at least 90% identity with SEQ ID NO:176, would be expected to exhibit a correspondingly high degree of immunological cross-reactivity with SEQ ID NO:176. The skilled artisan would further expect, based upon Applicants' disclosure, that a sequence of SEQ ID NO:176 could be modified using routine techniques to produce a polypeptide having at least 90% identity to a sequence of SEQ ID NO:176, and that these related sequences would similarly retain a high degree of immunological cross-reactivity with T cells that are specific for a polypeptide sequence of SEQ ID NO:176. These expectations on the part of the skilled artisan are submitted to be soundly based upon fundamental principles of immunological recognition and binding. In this regard, a precise disclosure regarding which specific amino acid residues of SEQ ID NO:176 can be modified while retaining the ability to stimulate T cells specific for an amino acid sequence of SEQ ID NO:176 is simply not necessary in this instance for a skilled artisan to practice the claimed invention when it would be well understood, in view of the instant disclosure, how to make and use the claimed sequences having at least 90% identity with SEQ ID NO: 176, and portions thereof, and how to determine whether the T cells elicited by such sequences are cross-reactive with an amino acid sequence of SEQ ID NO:176.

One of skill in the relevant art would further appreciate that there are a multitude of standard, art-recognized assays which one would use in order to confirm whether an immunogenic portion of a polypeptide having at least 90% identity with a polypeptide sequence of SEQ ID NO:176 would be capable of stimulating a T cell response cross-reactive with a sequence of SEQ ID NO:176 (*e.g.*, Example 7 and, in particular, Example 14, page 146, line 24-page 147, line 7). These well known assays include, by way of illustration, T cell proliferation assays and IFN-gamma production assays. Applicants submit that the use of such methods

amounts merely to routine screening and that such methods most certainly do not require undue experimentation.

Accordingly, as polypeptides having at least 90% identity with SEQ ID NO:176 or portions thereof would be understood to be capable of being made and used for stimulating T cells retaining specificity for the L523S sequence of SEQ ID NO:176, and as this would be well recognized as such by an artisan of ordinary skill, Applicants respectfully submit the claimed invention is indeed fully enabled by the specification as filed and could be practiced without undue experimentation and with a reasonable expectation of success.

With regard to the method claims, Applicants do not acquiesce to the former grounds of rejection, however, Applicants have canceled claims 13 and 14 and wish to defer these points to a later filed continuation application in which the claims in their original scope will be prosecuted. Thus, Applicants urge that the pending claims fully satisfy the enablement requirements of 35 U.S.C. § 112, first paragraph, and that the rejection of the claims under this section may be properly withdrawn.

Rejections Under 35 U.S.C. §§ 102(a) and 103(a)

Claims 20-23 stand rejected under 35 U.S.C. § 102(a) as allegedly anticipated by, or in the alternative under 35 U.S.C. § 103(a) as allegedly obvious over Chen *et al.*, WO 99/54738. In particular, the Action contends that Chen *et al.* teaches a composition comprising the cancer associated antigen, KOC-1, and a pharmaceutically acceptable adjuvant, and that this antigen, identical to the sequence of SEQ ID NO:176, induces antibodies when expressed in a subject.

Applicants respectfully traverse the rejection and submit that "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). Furthermore, "anticipation requires the presence in a single prior art reference disclosure of each and every element of the claimed invention, *arranged as in the claim*." *Lindemann Maschinenfabrik GmbH v. American Hoist & Derrick Co.*, 221 USPQ 481, 485 (Fed. Cir. 1984) (emphasis added).

Chen *et al.* teaches the identification of the polypeptide set forth in SEQ ID NO:176 using serological screening of a melanoma expression library. However, nowhere does Chen *et al.* teach that the polypeptide set forth in SEQ ID NO:176 or any portion or variant thereof is capable of stimulating T cells. Furthermore, this reference does not teach an immunogenic composition comprising the polypeptide of SEQ ID NO:176 or any portion or variant thereof and an adjuvant that induces a predominantly Th1-type response. Therefore, Applicants respectfully submit that Chen *et al.* does not anticipate the presently claimed invention.

Further, Applicants submit that without the knowledge that the claimed polypeptide is capable of eliciting T cells, as disclosed by Applicants in the present application, the skilled artisan would have had no motivation and it would not have been obvious to the skilled artisan, to combine the claimed polypeptide with an adjuvant that induces predominantly a Th1 type response. Accordingly, Applicants submit that the claimed invention is not obvious in view of Chen *et al.*

Applicants submit that the claimed invention is not anticipated or, in the alternative, obvious over Chen *et al.*, and respectfully request that the rejection under 35 U.S.C. § 102(a) or in the alternative under 35 U.S.C. § 103(a) be reconsidered and withdrawn.

The Commissioner is authorized to charge any additional fees due by way of this Amendment, or credit any overpayment, to our Deposit Account No. 19-1090.

Applicants respectfully submit that all the claims remaining in the application are now believed to be allowable. Favorable consideration and a Notice of Allowance are earnestly solicited.

Respectfully submitted,

Tongtong Wang *et al.*

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Enclosure:
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